

PATENT COOPERATION TREATY

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From the  
 INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

GENENTECH, INC.  
 LEGAL DEPT.

To:  
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**PCT**

NOTIFICATION OF TRANSMITTAL OF  
 INTERNATIONAL PRELIMINARY  
 EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
 (day/month/year) **30 SEP 2004**

Applicant's or agent's file reference

P1959R1

**IMPORTANT NOTIFICATION**

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US03/17697

04 June 2003 (04.06.2003)

07 June 2002 (07.06.2002)

Applicant

GENENTECH, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Mail Stop PCT, Attn: IPEA/US  
 Commissioner for Patents  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450

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Authorized officer

Amy Nelson

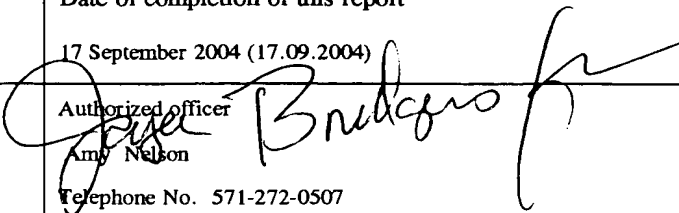
Telephone No. 571-272-0507

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br>P1959R1  | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)                          |   |
| International application No.<br>PCT/US03/17697   | International filing date (day/month/year)<br>04 June 2003 (04.06.2003)  | Priority date (day/month/year)<br>07 June 2002 (07.06.2002) |
| International Patent Classification (IPC) or national classification and IPC<br>IPC(7): A61K 67/00 and US Cl.: 800/008  |  |   |
| Applicant<br>GENENTECH, INC.  |  |   |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>—</u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"><li>I <input checked="" type="checkbox"/> Basis of the report</li><li>II <input type="checkbox"/> Priority</li><li>III <input checked="" type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</li><li>IV <input type="checkbox"/> Lack of unity of invention</li><li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li><li>VI <input type="checkbox"/> Certain documents cited</li><li>VII <input type="checkbox"/> Certain defects in the international application</li><li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li></ul> |  |   |
| Date of submission of the demand<br>29 October 2003 (29.10.2003)  | Date of completion of this report<br>17 September 2004 (17.09.2004)  |   |
| Name and mailing address of the IPEA/US<br>Mail Stop PCT, Attn: IPEA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (703) 305-3230   | Authorized officer<br><br>Amy Nelson<br>Telephone No. 571-272-0507 |   |

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-102 as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 103-116 as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☐ the drawings:  
pages NONE as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
pages NONE as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☐ The amendments have resulted in the cancellation of:**

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

**5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/17697

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 132-146

because:

- ☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 132-146

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.  
☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

|                               |                                 |     |
|-------------------------------|---------------------------------|-----|
| Novelty (N)                   | Claims <u>NONE</u>              | YES |
|                               | Claims <u>1-131 and 147-178</u> | NO  |
| Inventive Step (IS)           | Claims <u>NONE</u>              | YES |
|                               | Claims <u>1-131 and 147-178</u> | NO  |
| Industrial Applicability (IA) | Claims <u>1-131 and 147-178</u> | YES |
|                               | Claims <u>NONE</u>              | NO  |

**2. CITATIONS AND EXPLANATIONS**

Claims 1-11 lack novelty under PCT Article 33(2) as being anticipated by Tomlinson (Endocrinol., May 2002, Vol. 143, pages 1741-1747) or Nicholes (Am. J. Pathol. June 2002, Vol. 160, pages 2295-2307).

Tomlinson and Nicholes described the mouse of the instant disclosure (human FGF19 operably linked to a myosin light chain promoter; page 1742 of Tomlinson, page 2296 of Nicholes, pg 91 of the instant disclosure). The mouse of Tomlinson and Nicholes inherently had the characteristic claimed because it has the same structure as the mouse described in the disclosure.

Claims 1-131 and 141-148 lack novelty under PCT Article 33(2) as being anticipated by Botstein (US Pub. No. US 2002/0012961 A1, 31 January 2002).

Botstein taught a mouse whose genome comprised DNA encoding human FGF-19 (§ 178), cells isolated from the mice (§ 215), and using the mice to screen compounds (§ 217). The cancer cells can be introduced into the mice (§ 219), including hepatic carcinoma (§ 60).

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-11 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art.

The disclosure only describes how to use a transgenic mouse whose genome has DNA encoding FGF19 that has an increased likelihood of developing hepatic carcinoma as compared to a wild-type mouse. The state of the art was that it was not known how to stably incorporate a transgene into ES cells and obtain germline transmission in species other than mice. The disclosure does not teach how to make any transgenic mammal other than mice. The disclosure does not provide any correlative guidance between making transgenic mice and other mammalian species. If one of skill in the art could make other species of mammals, it was not predictable whether such species would have the same phenotype as the one found in mice. That is because it was unpredictable whether the phenotype obtained in mice could be obtained in other mammalian species. The disclosure does not provide any correlative guidance so that the ordinary artisan could obtain the results described with mice in other mammalian species.